

Please delete the paragraph on page 26, line 33 to page 27, line and replace it with the following paragraph:

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4.7 Entry into and exit from the proteasome particle

D2  
The hydrolytic activity of the proteasome is associated with Thr1 and the  $\beta$  ring surfaces in the interior of the  $\beta$  cavity that defines the hydrolytic chamber. The substrate must penetrate into the particle and the product must be released. In the case of the proteasome from *T. acidophilum* two entry openings with a diameter of about 1.3 nm are open at the ends of the cylindrical particles which are bordered by a ring surface of bend-forming segments Tyr126-Gly-Gly-Val (SEQ ID NO: 14) of seven identical  $\alpha$  subunits. The N-terminal residues 1 to 12 are disordered in this protein.

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**REMARKS**

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

In the event this paper is not considered to be timely filed, Applicant hereby petitions for an appropriate extension of time. The fee for this extension may be charged to our Deposit Account No. 01-2300, referring to client-matter number

100564-09039, along with any other fees which may be required with respect to this application.

Respectfully submitted,



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D. Daniel Dzara, II  
Registration No. 47,543

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Enclosure:    Marked-Up Copy of Specification

**MARKED UP COPY OF SPECIFICATION**

**Marked up version of the paragraph starting at page 9, lines 1-10 is below:**

Figure 1 shows the homology between the amino acid sequences **(SEQ ID NOS 1-13, respectively, in order of appearance)** from yeast and humans coding for the active subunits of the proteasome; the  $\beta$ 1/PRE3,  $\beta$ 2/PUP1,  $\beta$ 5/PRE2 subfamilies are indicated by the yellow, green and blue colour respectively; the residues of the S1 pocket which influence the specificity changes of the PRE3 subfamily after substitution of the human subunit Y by LMP2 after cytokine induction are shown in brown;

**Marked up version of the paragraph starting at page 26, line 33 to page 27, line 9 is below:**

**4.7 Entry into and exit from the proteasome particle**

The hydrolytic activity of the proteasome is associated with Thr1 and the  $\beta$  ring surfaces in the interior of the  $\beta$  cavity that defines the hydrolytic chamber. The substrate must penetrate into the particle and the product must be released. In the case of the proteasome from *T. acidophilum* two entry openings with a diameter of about 1.3 nm are open at the ends of the cylindrical particles which are bordered by a ring surface of bend-forming segments Tyr126-Gly-Gly-Val **(SEQ ID NO: 14)** of seven identical  $\alpha$  subunits. The N-terminal residues 1 to 12 are disordered in this protein.